AWARD NUMBER: W81XWH-09-2-0001

TITLE: Consortia for Improving Medicine with Innovation & Technology

PRINCIPAL INVESTIGATOR: John A. Parrish, M.D.

CONTRACTING ORGANIZATION: Massachusetts General Hospital Corporation
Boston, MA 02114

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Fort Detrick, Maryland 21702-5012

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4. TITLE AND SUBTITLE

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6. AUTHOR(S)

John A. Parrish, M.D.

email: mlender@partners.org

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The Consortia for Improving Medicine with Innovation & Technology (CIMIT) is a consortium of nonprofit Boston-area institutions based at Massachusetts General Hospital and includes Brigham and Women's Hospital, Massachusetts Institute of Technology, Draper Laboratories, Beth Israel Deaconess Medical Center, Boston Medical Center, Boston University, Boston Children's Hospital, Harvard Medical School, Newton-Wellesley Hospital, Northeastern University and VA Boston Healthcare System. The overall goal of CIMIT is to combine clinical and technological excellence and educational components to generate, develop, and reduce to practice innovative and high-impact concepts to improve military and civilian healthcare.

15. SUBJECT TERMS

Nothing listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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CIMIT®

Consortia for Improving Medicine with Innovation & Technology

Cooperative Agreement
W81XWH-09-2-0001

ANNUAL REPORT
Reporting Period
April 1, 2015 – September 30, 2015

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CIMIT Scientific Project Awards Supported by W81XWH-09-2-0001
Period ending September 30, 2015

F.O. Principal Investigator	Award Title	Fiscal Year	Award ID	CIMIT No.	Award Status
Ackerman, Jerome	Vascular Repair by MR Coagulation	2013	Out - 001834	13-1180	Partially Released
Agar, Nathalie	Intraoperative Stereotactic Molecular Imaging of Tumor Boundaries by Mass Spectrometry	2011	Out - 001577	11-216	Award Closed
Armoundas, Antonis	Advanced Pacing Methods for Preventing Life Threatening Arrhythmias	2011	Out - 001602	11-157	Award Closed
Bergethon, Peter	Multi-optode probe for evaluation of diabetic neuropathy	2009	Out - 000657	09-456	Award Closed
Bianchi, Matt	Telemedicine Strategy for Chronic Sleep Disorder Management	2013	Out - 001836	13-1240	Fully Released
Bickmore, Timothy	Optimizing Hospital Workflow and Quality through Patient Engagement	2012	Out - 001696	12-1035	Fully Released
Bizzi, Emilio	A Fully Autonomous Brain-Body Interface for Patients with Neuromuscular Injury or Disease	2011	Out - 001579	11-282	Award Closed
Blesius, Carl	Large Scale Learning Management/Competency Tracking System	2013	Out - 001840	13-2193	Fully Released
Bonato, Paolo	Combining galvanic vestibular stimulation and motor training in traumatic brain injury survivors with neglect	2010	Out - 000668	10-479	Award Closed
Borsook, David	Optical imaging for Rapid Determination of Pain: Field and Surgical Application	2014	Out - 001882	14-1882	Pending
Cash, Sydney	Microelectrode recordings and advanced algorithms for seizure prediction	2009	Out - 000691	09-325	Award Closed
Channick, Colleen	Creation of Amino Alcohol-Based Poly(ester amide) Elastomer Bioabsorbable airway Stent	2011	Out - 001580	11-401	Award Closed
Collins, John	Acceleration of Hand Hygiene Process Development and Manufacture	2011	Out - 001681	11-1681	Award Closed
Colson, Yolonda	Expansile nanoparticles for tumor-targeted drug delivery to prevent lymph node metastases in breast cancer	2010	Out - 000703	09-433	Award Closed
Cunningham, Miles	Optimizing Convection Enhanced Delivery of Therapeutics to Treat Intractable Epilepsy	2012	Out - 001716	12-1319	Award Closed
Dai, Tianhong	Antimicrobial Photodynamic Therapy for Prevention and Treatment of Surgical Site Infections	2013	Out - 001838	13-1021	Award Closed
Dai, Tianhong	Ultraviolet C Light for Prophylaxis and Treatment of Multi-drug Resistant Infections Associated with Burns in the Combat Casualty	2013	Out - 001839	13-1033	Award Closed
Del Nido, Pedro	Catheter-based adaptable device for closure of intracardiac defects in children	2011	Out - 001581	11-351	Award Closed
DeMoya, Marc	MGH Surgical Simulation Program	2013	Out - 001841	13-1307	Award Closed
Denis, Gerald	Ultrasound-directed delivery of cancer chemotherapeutic drugs	2009	Out - 000728	09-116	Award Closed

Dixon, Ronald	Healthcare 360: A technology-enabled model for general medical care	2009	Out - 000735	09-182	Award Closed
Duggan, Michael	Surviving Blood Loss Through Pharmacological Resuscitation	2014	Out - 001887	14-1887	Fully Released
Edelman, Elazer	Optimizing Tissue Engineering Therapies for Airway Injury in the Battlefield	2014	Out - 001883	14-1883	Fully Released
Elman, Igor	Novel predictors of pharmaco-therapeutic outcomes using functional reciprocity between heightened stress reactivity and emotional numbing in PTSD	2010	Out - 000749	10-515	Fully Released
Fennessy, Fiona	Computer-assisted tumor blood vessel tortuosity analysis at 3T, as a method of assessing ablative therapy response	2009	Out - 000755	09-359	Award Closed
Fregni, Felipe	Closed loop, detect-and-treat systems for epilepsy	2010	Out - 000765	10-522	Award Closed
Golby, Alexandra	A hybrid optic-electromagnetic surgical tool tip tracking system for neurosurgery	2010	Out - 000771	10-397	Award Closed
Goldman, Julian	PCA Monitoring Safety Interlock to Decrease Adverse Clinical Events	2011	Out - 001583	11-443	Award Closed
Goldman, Julian	Improving continuity of care for veterans by electronically exchanging MGH, VA, and DoD medical record data	2012	Out - 001714	12-1265	Award Closed
Gordon, James	Infrastructure for a National Simulation Proving Grounds: The CIMIT-Boston Simulation Consortium (Parotidectomy Surgical Simulator / Intraosseous Device Placement / Cricothyrotomy Model / Soft Tissue Simulant Rapid Prototyping	2013	Out - 001842	13-2191	Fully Released
Gordon, James	Low-cost, High-performance, Modular Patient Simulation System	2013	Out - 001843	13-2134	Fully Released
Gray, James	Using network analysis to improve the qualities of NICU care teams and their function	2011	Out - 001584	11-346	Award Closed
Guo, Lifei	A Novel Stent-Based, Sutureless Device for Rapid Vascular Anastomosis in Microsurgery	2010	Out - 001132	10-1132	Award Closed
Gupta, Rajiv	Dynamic Imaging and Neuro Intervention Guidance Using Dual Energy CT: Translation into Practice	2014	Out - 001884	14-1884	Fully Released
Guttag, John	A Novel Algorithm to Detect the End of a Seizure and the Post-Seizure Period	2011	Out - 001585	11-484	Award Closed
Hacking, Adam	Non-invasive Fasciotomy to Treat Extremity Compartment Syndrome	2012	Out - 001706	12-1173	Award Closed
Harris, N. Stuart	Novel Neuroimaging in Acute Mountain Sickness	2011	Out - 001586	11-306	Award Closed
Harris, N. Stuart	Early Time Course and Severity of Cerebral Edema and Acute Exposure to High Altitude	2010	Out - 001135	10-1135	Award Closed
Harris, R. Scott	Enhanced inhalation therapy for emphysema	2011	Out - 001587	11-341	Fully Released
Hata, Nobuhiko	Swimming capsule endoscope	2009	Out - 000806	09-368	Award Closed
Hauser, Carl	A Rapid PCR-Based, Point of Care Test To Discriminate Between Sterile and Infective SIRS	2011	Out - 001588	11-217	Award Closed

Hoge, Elizabeth	The Effect of Oxytocin on Fear Memory Consolidation: A Novel Intervention to Prevent PTSD	2011	Out - 001589	11-542	Award Closed
Hooper, David	Rapid Screening of MRSA-colonized Patients in the Ambulatory Setting	2012	Out - 001701	12-1082	Award Closed
Horng, Steven	Developing and validating an integrated intelligent sepsis monitoring system	2012	Out - 001713	12-1262	Award Closed
Howe, Robert	SEAS - CIMIT Medical Devices Graduate Design Course	2011	Out - 001683		Award Closed
Hung, Judy	Polymer injection for treatment of ischemic mitral regurgitation	2009	Out - 000814	09-331	Award Closed
Ingber, Donald	Microfluidic blood cleansing device for sepsis therapy	2010	Out - 000819	09-303	Award Closed
Kang, Dongkyun	Comprehensive microscopy for intraoperative margin assessment	2012	Out - 001693	12-1012	Award Closed
Karlinsky, Joel	Interoperability of Portable X Ray Machines with Ventilators in Monitored Settings	2011	Out - 001591	11-348	Award Closed
Karp, Jeffrey	A Drug Delivery Platform for Near Term Impact on Patient Care	2010	Out - 000837	10-592	Award Closed
Kaushal, Shalesh	Low Energy Laser as a Therapeutic for Dry Age-related Macular Degeneration	2011	Out - 001607	11-397	Award Closed
Kheir, John	Use of topical oxygen mirobubbles to enhance wound healing	2010	Out - 000841	10-453	Award Closed
Kreiman, Gabriel	Memory Alteration through Theta Phase-Locked Electrical Stimulation	2011	Out - 001578	11-109	Award Closed
Kumar, Sandeep	Non-invasive brain stimulation for improving stroke related dysphagia	2012	Out - 001708	12-1187	Award Closed
Lee, Yong-Tae	Improving Recovery after Stroke via Electrical Stimulation of Proprioceptors	2011	Out - 001593	11-397	Award Closed
Lev, Michael	EIS as an "EKG for the Brain": Portable Point-of-Care Detection of Acute Traumatic Hematoma	2012	Out - 001694	12-1031	Award Closed
Lim, Chun	Augmented reality glasses for the treatment of visuospatial neglect	2009	Out - 000870	09-120	Award Closed
Lin, Alexander	Neurochemical and Multimodal Biomarkers for Chronic Traumatic Encephalopathy	2011	Out - 001592	11-127	Award Closed
Little, Patrick	Xenon anesthetic - FY10 Student Project	2010	Out - 001093		Award Closed
Little, Patrick	Harvey Mudd College Student Research Project	2009	Out - 001094		Award Closed
Mavroidis, Constantinos	Smart Orthoses for Home Based Tele-Rehabilitation Systems	2012	Out - 001715	12-1278	Award Closed
Mazumder, Malay	Electrostatic dry powder inhaler for constant dose respiratory drug delivery	2010	Out - 000885	10-512	Award Closed
McLaughlin, Bryan	An implantable, wireless electrode derivation for chronic EEG recording in epilepsy	2010	Out - 000888	10-418	Award Closed
Moss, Frank	Collaborative Virtual Rehabilitation Interface with Home Treatment Integration	2011	Out - 001594	11-358	Award Closed
Newbower, Ronald	Handwashing compliance reminder and documentation	2009	Out - 000904	09-221	Award Closed
O'Donnell, Lauren	Diagnosis of diffuse axonal injury using robust tract-based quantification of diffusion tensor imaging	2011	Out - 001596	11-298	Award Closed

Orr, Scott	Event-related P2 slope as a predictor of response to SSRIs in a veteran population	2011	Out - 001597	11-189	Fully Released
Ottensmeyer, Mark	Improvements and User Testing of Modular Enhancements for Mannequin-based Medical Simulators	2013	Out - 001846	13-2130	Fully Released
Ottensmeyer, Mark	Low cost, modular enhancements for mannequin-based medical simulators	2012	Out - 001703	12-1126	Fully Released
Ottensmeyer, Mark	Eye trauma simulator	2010	Out - 000900	10-331	Award Closed
Pang, Trudy	Development of a Stat EEG Prototype for Rapid Diagnosis of Non-convulsive Status Epilepticus for Community Hospital Settings	2012	Out - 001709	12-1198	Fully Released
Pascual-Leone, Alvaro	Noninvasive, Physiologic Characterization of Cortical Plasticity After Mild Traumatic Brain Injury in Humans	2011	Out - 001598	11-490	Award Closed
Pascual-Leone, Alvaro	Near-infrared photobiostimulation as a means of neuromodulation in stroke	2009	Out - 000921	09-153	Award Closed
Patz, Samuel	Magnetic Resonance Pulmonary Edema Monitor	2013	Out - 001847	13-1156	Fully Released
Pelton, Stephen	Development of safe and effective novel transtympanic membrane strategy for treatment of acute bacterial otitis media	2009	Out - 000923	09-330	Award Closed
Pollock, Nira	Development of a Novel Paper-based Point-of-care Test for Liver Function	2011	Out - 001572	11-141	Award Closed
Poznansky, Mark	A cutaneous laser system for augmenting the immunogenicity of HIV vaccines	2010	Out - 000930	10-394	Award Closed
Raemer, Daniel	Development of a Surgical Hemmorrhage Control Training Simulator	2013	Out - 001849	13-1024	Award Closed
Rattner, David	Natural orifice translumenal endoscopic surgery (NOTES)	2010	Out - 000934	08-442	Award Closed
Rattner, David	Natural orifice translumenal endoscopic surgery (NOTES)	2009	Out - 000938	08-442	Award Closed
Redmond, Robert	Optimal Time and Method of Repair of Peripheral Nerve Injury Involving Nerve Deficit	2013	Out - 001856	13-1856	Award Closed
Redmond, Robert	Preventing Leakage from Colon Anastomosis Sites	2011	Out - 001599	11-184	Award Closed
Redmond, Robert	A photo-activated nanofiber graft material for enhanced tendon repair	2010	Out - 000941	10-193	Award Closed
Reisner, Andrew	Identification of life-threatening conditions in trauma patients by automated processing of vital signs data	2011	Out - 001718	11-1718	Fully Released
Reisner, Andrew	Automated processing of physiologic registry for assessment of injury severity (APPRAISE BMF)	2011	Out - 001668	09-509	Award Closed
Rotenberg, Alexander	A novel application of intranasal Huperzine A in treatment of traumatic brain injury	2011	Out - 001600	11-269	Award Closed
Rotenberg, Alexander	A Novel Metric of HuperzineA Pharmacodynamics Efficacy	2014	Out - 001885	14-1885	Fully Released
Sacco, Dianne	Advanced Ureteroscope Navigation System for Calculi Removal	2011	Out - 001603	11-442	Award Closed

Saukkonen, Jussi	Low-Cost, Low Maintenance Mechanical Ventilator for Developing World or Mass Casualty	2011	Out - 001606	11-169	Award Closed
Saukkonen, Jussi	Development of an interactive, clinical algorithm-driven interoperable smart ventilator	2011	Out - 001604	11-251	Award Closed
Schlaug, Gottfried	TDCS - stroke recovery	2009	Out - 000959	09-392	Award Closed
Shenton, Martha	Improving Imaging of Diffuse Axonal Injury in Traumatic Brain Injury	2011	Out - 001608	11-539	Award Closed
Sheridan, Roberto	Endotracheal tube imaging device	2009	Out - 000965	09-348	Award Closed
Sipahi, Rifat	Building Handheld Devices to Accommodate Essential Tremor	2012	Out - 001711	12-1230	Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2012	Out - 001733		Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2011	Out - 001647		Award Closed
Slocum, Alexander	MIT- CIMIT Precision Medical Devices Graduate Design Course 2.75	2014	Out - 001911		Fully Released
Slocum, Alexander	MIT-CIMIT Precision Medical Devices Graduate Design Course 2.75	2009	Out - 001097		Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2010	Out - 001099		Award Closed
Spector, Jonathan	Resuscitation technology for saving newborn lives	2010	Out - 000978	10-240	Award Closed
Sridhar, Srinivas	Multi-Modal Imaging Nanoplatforms for Image-Guided Therapies	2013	Out - 001857	13-1087	Award Closed
Subramaniam, Balachundhar	Echocardiography guided central oximetry	2011	Out - 001609	11-457	Award Closed
Teng, Yang	Treatment of Spinal Cord Injury Pain with Huperzine A: A Pre-clinical Study	2011	Out - 001614	11-527	Award Closed
Teng, Yang	Carbon monoxide mediated neural protection for treating spinal cord injury	2011	Out - 001613	11-532	Award Closed
Thompson, Christopher	Utilization of a Novel Kinematics System to Improve Quality in Colonoscopy	2011	Out - 001610	11-291	Award Closed
Tokuda, Junichi	Robot-assisted laparoscopic prostatectomy guided by patient-specific models	2011	Out - 001611	11-325	Award Closed
Tolkoff, Josh	Automated Capillary Refill Detector: Hydration Monitor	2011	Out - 001687	11-1687	Award Closed
Toner, Mehmet	A label-free viral detection microchip for point-of-care applications	2010	Out - 000999	09-440	Award Closed
Tullius, Stefan	A system to measure continuous flow and perfusion to ensure successful kidney transplantation	2010	Out - 001008	10-582	Award Closed
Unlu, M. Selim	BU/CIMIT Applied Healthcare Engineering Fellowship 2009 Projects	2009	Out - 001103		Award Closed
Uygun, Korkut	High Efficiency Hepatocyte Isolation System	2012	Out - 001732	12-1732	Fully Released
Vakoc, Benjamin	An image-guided laser therapy catheter for Barrett's esophagus	2010	Out - 001019	10-480	Award Closed
Weiner, Debra	Handheld simulation procedure training device	2010	Out - 001041	10-179	Fully Released
Weinstock, Peter	Development of an integrated child circulatory system simulator to enhance patient safety via procedural skills and team training in pediatrics	2010	Out - 001043	10-225	Award Closed
Wilson, Kim	Using Mobile Electronic Protocols to Improve Newborn Survival in Developing Country Settings	2011	Out - 001605	11-233	Award Closed

Winograd, Jonathan	Immediate Restoration of Transected Peripheral Nerves with Polyethylene Glycol and Methylene Blue (PEG/MG Fusion)	2013	Out - 001850	13-1144	Award Closed
Yarmush, Martin	Development of Immuno -Therapy Laden Scaffolds for the Prevention of Post-Burn and Traumatic Injury Infection to Enhance Wound Healing and Repair	2012	Out - 001695	12-1034	Award Closed
Yoo, Seung-Schik	Direct functional brain mapping using image-guided focused ultrasound	2010	Out - 001064	10-142	Award Closed
Yun, Seok-Hyun	Dynamic cross sectional and functional imaging of vocal folds (4D laryngoscopy)	2010	Out - 001068	10-106	Award Closed
Yun, Seok-Hyun	Novel ocular biomechanical analysis	2009	Out - 001069	09-148	Award Closed

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Telemedicine Strategy for Chronic Sleep Disorder Management
Principal Investigator:	Matt Bianchi
CIMIT Project No.:	13-1240
This is a:	[X] Progress Report [ ] Final Report
Report Period: *	to September 30, 2015
Report Period Ending:	September 30, 2015

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

This project has been approved for re-purposing, and is now called "Sleep disorder system development for predictive analytics".

Aim 1: To optimize algorithms for apnea detection and sleep quality based on respiration patterns.
We have recently shown that apnea detection is feasible using only respiratory movements in a small cohort of 100 patients[1]. To demonstrate that this technique can generalize across diverse patient populations, we propose to use machine learning methods applied to a large database of 3000 patients from the MGH Sleep Lab. We will implement this system via a web-based platform to manage and display respiration data outputs.

Aim 2: To validate lab-based algorithms using respiration data obtained in the field with home-monitoring devices
We have collected home-based data using smart-shirt and smart-belt devices that record respiration over multiple nights, in subjects with and without OSA. Our ongoing studies (funded independently) continue to feed this important database of field data, to determine the extent to which our lab-based optimizations (Aim 1) can generalize to the home setting.

Aim 3: Ongoing development and selection of Respiration Monitoring 'wearables' and associated data extraction.
We will compare alternative devices (Mimo from Rest Devices, BioHarness from Zephyr, Equivital from Respironics, and the Hexoskin smart shirt) regarding key technology aspects. We have purchased these devices from other funds and will focus on algorithm-relevant analysis of our field acquired experiences.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We have collected in-lab and at-home data from 25 patients (1 lab, 3 home, each), and are in the process of analysis. We project to complete the remaining 25 patients by June 30th.
We have identified an outside consultant for implementing the architecture of our Sleep Apnea Monitoring (SAM) system, which consists of data import and management, algorithm implementation, display, and export.
Algorithm development is advancing on two fronts: 1) completing database creation to allow optimization across a variety of clinical factors (as OSA is a very heterogeneous disease). We have exported over 2000 PSGs to date (goal is 3000 by June 30th); 2) parameter

optimization: we are now comparing methods and optimizing computational time to allow our multi-step algorithm to function quickly, so it can be implemented in real time using the SAM system. For example, in under 60 seconds we can run pre-processing, movement detection, and apnea detection, on a full night of respiration data. Further improvements are expected in terms of computational efficiency.

Sept 30 update: We have completed the initial analysis of n=50 subjects (1 lab night, 3 home nights, for each one), and find excellent recording fidelity in the lab, somewhat more variable in the home (ie, with self-application of the monitor), and are in the process of validating movement and apnea detection algorithms on this complete set. We have exported over 3000 PSGs from our existing database, and are in the process of cleaning this set (e.g., aligning the raw files with the scored annotations, verifying file lengths and integrity, etc). We have completed the initial version of the SAM system with an outside consultant for web design, which consists of a web interface, uploading and launching MATALB executable files, display and scroll/zoom features, and output pages for summary data of clinical relevance.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

Algorithm performance turns out to be very sensitive to signal features in the amplitude domain, which can change within a night, as well as across subjects. We are creating a form of windowed normalization to address this, and will need to have a parallel "QA" step in the algorithm to identify minimal requirements of the signal amplitude and resolution to ensure algorithm performance (ie, identify data quality limits).
We have also been delayed in obtaining raw data from the mattress pad and non-contact devices, which require special export capability from the companies making them. Active conversations with ResMed, Beddit, and Withings are underway – each is willing to share the raw data, but this step has not yet materialized. Other devices do allow raw analysis (Zephyr, Hexoskin, Equivital, RestDevices).

Sept 30 update: We have obtained raw data from several devices, including ResMed S+ and the Beddit, with the former being more cumbersome, so we have focused on the latter. We have compared the beddit signal with ResMed and Zephyr and the belts from the lab PSG, and find them of sufficient quality to proceed with further development of SAM using the beddit as the source of data, rather than the zephyr, for operational reasons (zephyr requires re-charge and data-transfer after every night, and needs to be worn – beddit is passive, plugs into the wall, and transfers data to a server daily). Finally, from an algorithm standpoint, we have markedly advanced our analysis approach to deal with the issues previously mentioned, namely multi-scale normalization, envelope tracking, and feature selection. Further optimization is ongoing. Data quality metrics are in place and reliable.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

1) Continue PSG exports to reach our 3000 goal
   (Sept 30 update: we have met this goal, and continue to expand and clean our retrospective database for algorithm optimization)
2) Complete enrollment of remaining 25 patients for the in-lab vs at-home validation of respiration monitoring
   (Sept30 update: we have completed all 50 patients for this protocol)
3) Parameter optimization for initial dataset by June 30
   (Sept30 update: we are still working on algorithm optimization)
4) Cross validation on wider dataset by Sept 30
   (Sept30 update: expanded cross validation awaits #3)
5) Apply QA methods to each wearable (mattress pad, shirt, belt, etc): this is key to determine whether our algorithm is inter-operable across devices (compared to the main validation which is on the gold-standard belts)
   (Sept30 update: data quality has been confirmed for beddit, but not the S+)

6) Application for R01 (June deadline) to utilize the SAM system for a novel sleep apnea application related to clinical effectiveness and apnea burden in treated OSA patients.
(Sept30 update: we have postponed grant application to this winter, for the apnea burden submission; we did apply for two foundation grants regarding sleep apnea and home device monitoring validation, and await decisions on Dec 1)

V. Presentations:

Dr Bianchi has presented preliminary algorithm results at the international World Association of Sleep Medicine in South Korea
(Sept30 update: we have made local presentations at MGH events)

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

None to date

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

None to date

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

None to date

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

6 Please enter a value between 2 and 10 see Technology Readiness Levels, below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

We have tested wearables in human subjects against the gold standard PSG (in-lab), and feasibility of recordings at home as well (items 4 and 6). We have shown that the portable Zephyr belts, and application of basic algorithms to belt data, is equivalent to the gold standard belts used in clinical PSG.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Surviving Blood Loss Through Pharmacological Resuscitation
Principal Investigator:	Michael Duggan
CIMIT Project No.:	14-1887
This is a:	[X] Progress Report [ ] Final Report
Report Period: *	to September 30, 2015
Report Period Ending:	September 30, 2015

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

Overall objectives are to determine whether VPA (300 mg/kg or 150 mg/kg) works synergistically with hypertonic saline to improve cell survival following trauma and hemorrhagic shock in a large animal model.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

After receiving tissues from the Massachusetts General Hospital, we have studied acute lung injury (ALI) by scoring the severity of alveolar congestion and hemorrhage, infiltration of neutrophils in the air spaces or vessel walls, and the thickness of alveolar wall/hyaline membrane formation. The scoring of ALI was performed by a board certified pathologist blinded to the treatment assignment of the samples, as we described previously (Liu *et al*. Shock. 2014; 41: 104-108). We found that either normal saline (NS) or hypertonic saline (HTS) has no effect on ALI in the swine model of poly-trauma and hemorrhage. However, addition of VPA into HTS significantly decreased the injury, compared to the group of NS or HTS alone ($p < 0.05$). We demonstrated for the first time, in a large animal model of severe hemorrhagic shock with multiple organ injury, that VPA can decrease acute lung injury.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

None

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

We will determine how VPA can attenuate trauma/hemorrhage induced ALI, by assessing the lung tissues for (1) whether VPA inhibits neutrophil activation, (2) whether VPA induces protein acetylation, (2) whether VPA decreases inflammatory cytokine production, and (4) whether there is a biomarker in the treatment of ALI with VPA.

V. Presentations:

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

http://www.ncbi.nlm.nih.gov/pubmed/25323999

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

N/A Please enter a value between 2 and 10 see Technology Readiness Levels, below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Dynamic Imaging and Neuro Intervention Guidance Using Dual Energy CT: Translation into Practice
Principal Investigator:	Rajiv Gupta
CIMIT Project No.:	14-1884
This is a:	[X] Progress Report [ ] Final Report
Report Period: *	April 1, 2015 to September 30, 2015
Report Period Ending:	September 30, 2015

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

The objective of our study is to improve the outcome of patients with Intracranial hemorrhage (ICH). ICH can be occurred in brain parenchyma or meningeal spaces. ICH is commonly encountered in combat care due to head trauma. A number of cases of ICH can be managed conservatively, a significant proportion of cases of ICH can progress rapidly in size and become life threatening. Hematoma expansion in patients ICH is strongly associated with increased morbidity and mortality.

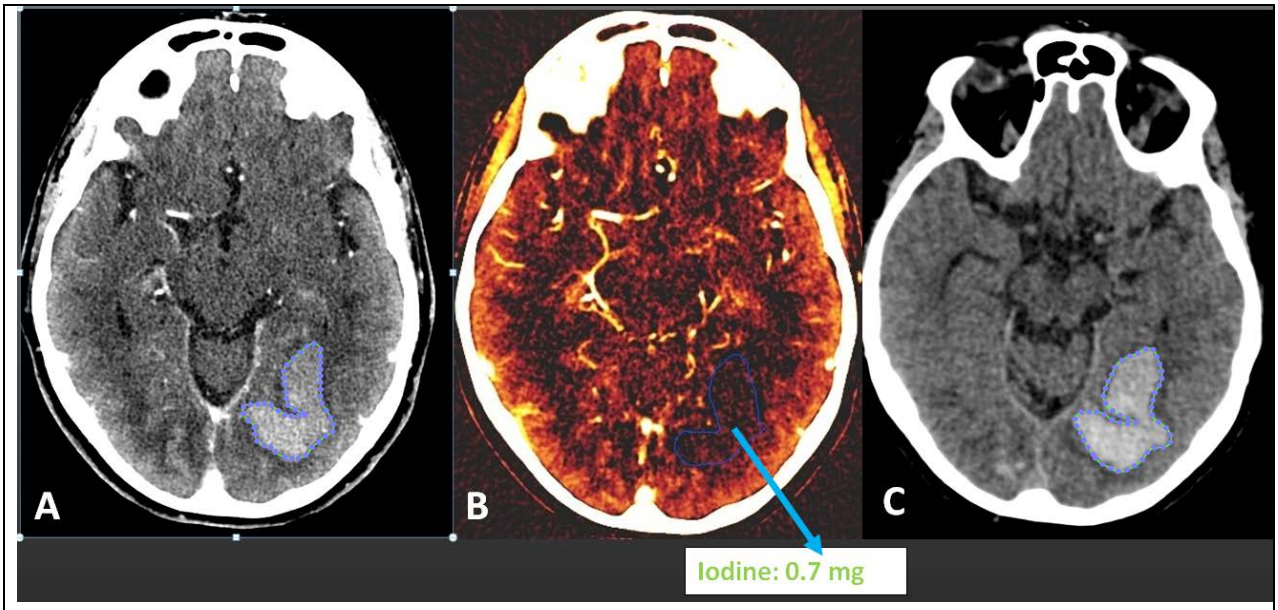
The “spot sign” is the presence of active leakage of iodinated contrast from the vessels. It has been shown to be an indicator of ongoing bleeding and, as such, an accurate and powerful predictor of hematoma expansion, mortality, and poor outcome. The specific aim of this study is to develop a new methodology using Dual Energy CT (DECT) to predict ICH that is likely to increase in size.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

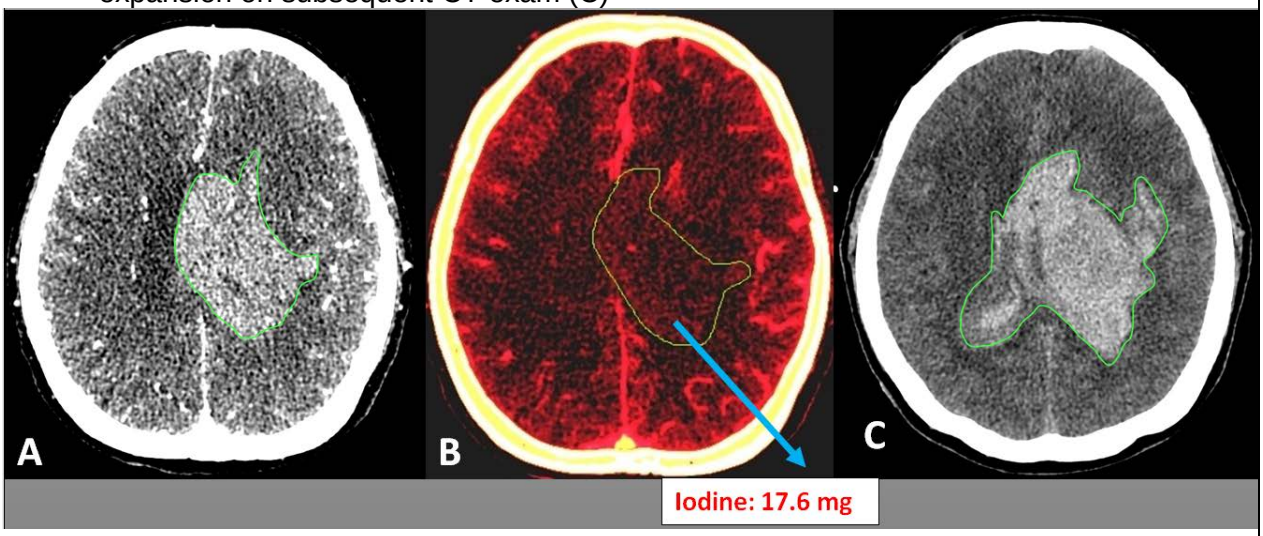
To this date, 13 patients with intra-parenchymal hemorrhage have undergone DECT angiography of the head in the emergency department. Of these, 8 patients met the inclusion criteria and had follow up head CT. The amount of iodine in the hematoma and the volume of the hematoma have been measured in these 8 cases.

We have submitted the results these cases and presented our scientific poster at Military Health System Research Symposium (MHSRS) annual meeting 2015. The study results showed that DECT material decomposition can accurately differentiate between calcification and hemorrhage in patients presenting for emergency head imaging, and can help correctly classify the lesions that may be misinterpreted by single energy image alone. In addition, DECT may enables iodine measurement within an intra parenchymal hematoma and the quantity of extravasated contrast may be a predictor of the hematoma expansion. Here are few cases showing relation of iodine concentration on DECT delayed exam and hematoma expansion on subsequent CT exam.

1. Minimum iodine concentration (0.7 mg) on delayed DECT images (B) and no hematoma expansion on subsequent CT exam (C)



2. Higher iodine concentration (17.6 mg) on delayed DECT images (B) and hematoma expansion on subsequent CT exam (C)



III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

First, IRB requires us to prospectively obtain patient's or surrogate's permission to use and analyze the data. We have found this to be difficult in the clinical environment surrounding acute ICH in the emergency department. Many times the patient is not in a physical condition to understand the requirements of the study and give informed consent. At the same time, a surrogate is not available to given informed consent for enrollment at the time of the scan.

This study does not require any change in the default clinical scan protocol, or any other alteration in the clinical care of patient. The patients are ordered for a DECT scan based on the clinical necessity. Given that the data is analyzable retrospectively, we have requested the IRB to allow us to enroll these patients retrospectively as a part of a retrospective study that analyzes the data that has already been acquired. A new retrospective protocol linked to the original one.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

So far, we have performed DECT exams in 13 patients. Our goal is to enroll 20 eligible patients and measure the amount of iodine and volume of the hematoma in each patient. We hope that DECT will better demonstrate early extravasation of iodine contrast, and this surrogate marker will be a more accurate predictor of hematoma expansion in ICH.

Recently, we have made dual energy delayed CT of the head at 90 seconds as a default protocol for ICH assessment in our hospital. This change would allow assessing DECT protocol for large number patients with ICH. In addition, we have written the MATLAB program to replicate the similar region of interest (ROI) from one image series (DECT virtual non-contrast) to another image series (DECT Iodine). Identical ROI will allow us to compare the objective measurement (CT numbers, image noise, iodine) between different image series. The difference in the objective measurement would allow us to assess the extravasations of intra-cerebral hematoma.

After the initial validation of the hypothesis that DECT can predict hematoma expansion, phase II of this project will target performing this study on a single energy scanner, the type that is likely to be available in the field. We will also try to further propagate the DECT methodology to military facilities where a dual energy scanner is available.

V. Posters and Presentations:

1. Daftaribesheli L, Hu R, Young J, Padole A, Wu M, Pomerantz S, Romero J, Lev M, Gupta R. The Efficacy of Dual Energy CT in Characterizing Intracranial Hemorrhage in the Setting of Acute Head Trauma. Military Health System Research Symposium (MHSRS) 2015.

1. Daftaribesheli L, Ahmadi E, Khalilzadeh O, Gupta R. Application of the dual energy CT scan for differentiation of parathyroid gland from thyroid gland based on enhancement characteristics. Oral presentation in Radiology Society of North America (RSNA), Chicago, December 1-6, 2014.

2. Daftaribesheli L, Mayich MS, Ginat DT, Gupta R. Clinical applications of dual energy CT in head and neck imaging. Poster presentation in Radiology Society of North America (RSNA), Chicago, December 1-6, 2014.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

1. Ginat DT, Mayich M, Daftari Besheli L, Gupta R. Clinical applications of dual energy CT in head and neck imaging. Accepted for publication in Head & Neck, 2014

2. Dinkel J, Catherine PM, Khalilzadeh O, Goenka AH, Yoo A, Hirsch J, Gupta R. Technical limitations of Dual Energy CT in neuroradiology: 30 months institutional experience and review of literature. Journal of neurointerventional surgery.

3. Aran S, Besheli LD, Karcaaltincaba M, Gupta R, Flores EJ, Abujudeh HH. Applications of Dual-Energy CT in Emergency Radiology. AJR Am J Roentgenol. 2014 Apr;202(4):W314-24.

4. Won SY, Schlunk F, Dinkel J, Karatas H, Leung W, Hayakawa K, Lauer A, Steinmetz H, Lo EH, Foerch C, Gupta R. Imaging of Contrast Medium Extravasation in

Anticoagulation-Associated Intracerebral Hemorrhage With Dual-Energy Computed Tomography. Stroke. 2013 Aug 6.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

A static CT concept proposal submitted as a part of the CIMIT DoD Joint War Fighter Proposal.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

4 Please enter a value between 2 and 10

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

The proof of concept has been demonstrated previously by our research. This project, if successful, will bring this concept from TRL 3 to TRL 4.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Enhanced Inhalation Therapy for Emphysema
Principal Investigator:	Robert Scott Harris
CIMIT Project No.:	11-341
This is a:	[x] Progress Report [ ] Final Report
Report Period: *	to September 30, 2015
Report Period Ending:	September 30, 2015

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

Project Overview: It was proposed to design and build a small proof-of-concept device to enhance the delivery of aerosol drugs to the emphysematous lung. The device sends pressure pulses deep into the lung as the user exhales through it. In this CIMIT project the device will be evaluated in a limited number of studies assessing its effect for reducing hyperinflation, and its capacity to enhance ventilation distribution in emphysematous patients.

Specific Goals: 1) To design and build a novel, small proof-of-concept RPP delivery device **2)** to use that device in a limited number of studies to evaluate its efficacy for reducing global and regional hyperinflation, and enhancing ventilation distribution.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We worked extensively with the RPP device to ensure that the generated pressure waveforms are similar to those used in the Columbia study 30 years ago. We also modified the device to make sure that reliable measures of inspiratory capacity will be obtained. At present the device is ready for the first proof of concept study.

We ran into some issues with the RPP when we went to test the set-up prior to enrolling subjects with regard to the pressure waveform, which took some time to correct. We have now corrected this problem and are ready to test the device again in a mock-up and then, if successful, start recruiting subjects.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

We will finish recruiting and proceed with the measurements in the 10 subjects.

V. Presentations:

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

VII. **Enabled Funding:** Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

VIII. **Patent Disclosures and Filings:** Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

The device was Disclosed to the Partners TLO in November 2012. The disclosure is titled "Reverse Pressure Pulse Generator" and is listed as MGH File No. 21949 (Q&B 00584). The inventors listed on the disclosure are Elliot Greenblatt Jose Venegas, and Scott Harris.

The TLO has filed a provisional patent for the device.

IX. **Technology Readiness Level:** Assess the stage of development that best describes your solution at this current time.

5 Please enter a value between 2 and 10

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Development of Stat EEG Prototype and Clinical Protocol for Rapid Diagnosis of Nonconvulsive Status Epilepticus in the Emergency Setting
Principal Investigator:	Trudy Pang
CIMIT Project No.:	12-1198
This is a:	[ ] Progress Report [x] Final Report
Report Period: *	
Report Period Ending:	March 31, 2015

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

Status epilepticus (SE) is a neurological emergency which requires prompt diagnosis and treatment to avoid significant morbidity and mortality. Definitive diagnosis relies upon a high index of suspicion and readily identifiable electrographic discharges on an electroencephalogram (EEG). Unfortunately, most hospitals, including Beth Israel Deaconess Medical Center (BIDMC) and its affiliated community hospitals, do not have a standardized protocol in place to identify and evaluate patients at risk for SE. To address this problem, we developed a clinical protocol combined with a simplified EEG system which can be placed on the patient with minimal training on the device and preparation of the patient's scalp.

A set of simplified EEG electrodes will be integrated with a portable EEG recorder for rapid EEG acquisition and uploading to a central EEG server. The central server will be remotely accessible for immediate interpretation by an on-call epileptologist who can then communicate the results to requesting ED physician to guide clinical care.

The project is divided into two phases: Phase 1 will focus on EEG prototype development, clinical pathway development, and simulation testing. Phase 2 will focus on evaluation of feasibility of implementation of the prototype and its performance.

Specific aims include:

1. Develop a simplified stat EEG prototype with a quick-start and auto-stop feature and develop a mechanism for EEG transmission to a secure on-line and remotely accessible server.
2. Develop a clinical care protocol for the evaluation of patients at risk for NCSE in the ED.
3. Implementation and evaluation of the performance of the stEEG prototype and the clinical care protocol in the ED in the evaluation of patients with suspected NCSE.
4. Implementation of the EEG prototype in an ambulatory setting.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project. **Progress on Specific Aims**

Aims 1 and 2 are completed.

Aim 1 took longer than expected due to a number of issues with developing the prototype and creating a system that allows real time review to ensure adequate quality of the EEG. The second major delay was gaining access to the hospital high speed wireless network for EEG transfer. The final major delay was in establishing remote review capabilities by setting up Digiview software on the Citrix server to allow reviewers to read studies from anywhere in the hospital and at home without the need for a portable reviewer.

Aim 3: Implementation and evaluation of the performance of the stEEG prototype and the clinical care protocol in the ED in the evaluation of patients with suspected NCSE.

After successful simulation of the use of the prototype in the EEG lab and ED and obtaining BIDMC IRB approval, we have started evaluating patients with altered mental status or suspected seizures with either the StatNet EEG or the Conventional EEG. We have demonstrated feasibility of implementation and are evaluating the performance of the prototype EEG system and the clinical protocol. The goal is to recruit 15 patients in each group. So far, we have successfully enrolled 14 patients in the conventional EEG group and 10 patients in Statnet group. The study was temporarily delayed due to temporary unreliability of the BIDMC hospital wireless data transfer capability. The hospital wireless system has recently been upgraded and allowed us to transfer EEG with good reliability. Another source of delay was related to the need for upgrading and maintenance of the DigiTrace EEG recorder by the company which required 6 weeks. We are actively enrolling an additional 5 patients in the StatNet EEG group and 1 patient in the conventional group to meet our target. There are 2 studies in the ED that are competing for similarly medical ill patients with altered mental status. Following this, we will need to compare the time delay in the two groups, as well as the quality of the recorders by blinded certified electroencephalographers. We have demonstrated both feasibility and statistically significant time advantage of using the StatNet electrodes.

March/15 Update:
We are in the process of writing up the manuscript for publication.

Aim 4: Implementation of the EEG prototype in an ambulatory setting.

Finally, as a proof-of-concept that the prototype may be suitable for outpatient use, we intend to send the system home with a volunteer and his/her caregiver, to demonstrate feasibility of use by the caregiver in the home and sending the study for remote EEG review.

March/15 update:
We have considered piloting this in the ambulatory setting, but after

discussion with our research staff and EEG staff, we have determined that the prototype as it is currently is too premature for use by patients at home. Further simplification of the system needs to be done before patients and caregivers can operate it with ease.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

Recruitment has been slower than anticipated due to competing studies in the ED that are also enrolling medically ill patients and many of those have altered mental status. The RA for the study is vigilant about approaching those patients early who may benefit from an urgent EEG.

March/15 update: enrollment is complete.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

Once the above study is complete and we can demonstrate feasibility and safety within the BIDMC, we would like to enroll a volunteer and his/her caregiver to take the prototype home to record an outpatient EEG for immediate review.

March/15 update:

Based on the feasibility and our results, we have taken the system to Beth Israel Deaconess Hospital – Needham campus as a pilot use. We were able to train the ICU and ER nurses on the use of the system. They have successfully recorded 3 EEGs on 3 unique patients. We have been able to review the 3 clinical studies remotely to assist with clinical care. We are currently working with Needham hospital implement the system clinically for standard routine use given they have very limited access to an EEG technician and board certified epileptologists. Once we can establish standard use, we will use this as a model to expand its use to other affiliated community hospitals.

V. Presentations:

Neurology faculty seminar series – presented preliminary data regarding feasibility and time delays between the Statnet and Conventional EEG groups.
Emergency room staff seminar series.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

None.

March/15 update:

Manuscript in preparation.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

None

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

None

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

9 Please enter a value between 2 and 10

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.